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## Inhaled corticosteroid dose-response on blood eosinophils in asthma

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## Inhaled corticosteroid dose response on blood eosinophils in asthma

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To the editor:

We read with interest the article by Price et al <sup>1</sup> showing a clear association between asthma control and a spot measurement of blood eosinophils. The mean beclometasone equivalent inhaled corticosteroid (ICS) dose in their cohort was 219ug/day. It is important to consider the dose response relationship of ICS dose on blood eosinophils. There is evidence of a dose response effect of ICS on reduction of blood eosinophils and eosinophilic cationic protein (ECP) for beclometasone equivalent ICS doses of up to 800ug/day.<sup>2-4</sup> In terms of mechanism it appears that dose related reduction in blood eosinophils and ECP by ICS is disconnected from commensurate adrenal suppression,<sup>3,5</sup> suggesting that systemic bioavailability of ICS may not be the principal cause of suppressing blood eosinophils.

The data from Price et al <sup>1</sup> were somewhat conflicting showing that patients on step 4 therapy with high dose ICS had a 13% increased likelihood of having a blood eosinophil count >400 cells /uL, which was not observed for step 3 patients who were also taking  $\geq$  800ug/day beclometasone equivalent ICS dose, while step 2 patients on low dose ICS were 8% less likely to have a raised count. However we appreciate that it might be difficult to dissect out the suppressive effects of ICS on eosinophils per se from the ICS dose being a proxy for associated asthma severity. Titrating ICS dose over 1 year against mannitol airway hyper-responsiveness,<sup>5</sup> results in reduced exacerbations, improved symptom control and reduced reliever use, accompanied by a 34% fall in ECP. The relative suppression of eosinophils and ECP in response to 400ug/day beclometasone equivalent ICS dose is 23% and 17% respectively for blood and 76% and 55% for sputum,<sup>6</sup> inferring that sputum is more

sensitive, although it is less practical. In this regard it has been shown that titrating ICS against sputum eosinophils results in reduced exacerbations and associated AHR.<sup>7</sup> It would therefore be relevant to know if using serial blood eosinophils to adjust the ICS dose might result in reduced exacerbations, especially in patients who already have an optimised asthma control questionnaire score  $<0.75$ <sup>8</sup> at the time when the eosinophil count is measured.

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## References

1. Price DB, Rigazio A, Campbell JD, et al. Blood eosinophil count and prospective annual asthma disease burden: a UK cohort study. *Lancet Respir Med* 2015.

2. Anderson WJ, Short PM, Williamson PA, Lipworth BJ. Inhaled Corticosteroid Dose Response Using Domiciliary Exhaled Nitric Oxide in Persistent Asthma The FENotype Trial. *Chest* 2012; **142**(6): 1553-61.
3. Anderson WJ, Short PM, Williamson PA, Manoharan A, Lipworth BJ. The inverse agonist propranolol confers no corticosteroid-sparing activity in mild-to-moderate persistent asthma. *Clin Sci (Lond)* 2014; **127**(11): 635-43.
4. Wilson AM, Lipworth BJ. Dose-response evaluation of the therapeutic index for inhaled budesonide in patients with mild-to-moderate asthma. *American Journal of Medicine* 2000; **108**(4): 269-75.
5. Lipworth BJ, Short PM, Williamson PA, Clearie KL, Fardon TC, Jackson CM. A randomized primary care trial of steroid titration against mannitol in persistent asthma: STAMINA trial. *Chest* 2012; **141**(3): 607-15.
6. Currie GP, Syme-Grant NJ, McFarlane LC, Carey FA, Lipworth BJ. Effects of low dose fluticasone/salmeterol combination on surrogate inflammatory markers in moderate persistent asthma. *Allergy* 2003; **58**(7): 602-7.
7. Green RH, Brightling CE, McKenna S, et al. Asthma exacerbations and sputum eosinophil counts: A randomised controlled trial. *Lancet* 2002; **360**(9347): 1715-21.
8. Juniper EF, Bousquet J, Abetz L, Bateman ED, Committee G. Identifying 'well-controlled' and 'not well-controlled' asthma using the Asthma Control Questionnaire. *Respir Med* 2006; **100**(4): 616-21.